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Pesticide Fact Sheet Number 18: Thiodicarb

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This document contains up-to-date chemical information, including a summary of the Agency's regulatory position and rationale, on a specific pesticide or group of pesticides. A Fact Sheet is issued after one of the following actions has occurred.

1. Issuance or reissuance of a registration standard,
2. Issuance of each special review document,
3. Registration of a significantly changed use pattern,
4. Registration of a new chemical, or
5. An immediate need for information to resolve controversial issues relating to a specific chemical or use pattern.

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b. Identifiers/Open-Ended Terms

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EPA

Pesticide Fact Sheet

Name of Chemical: Thiodicarb
Reason for Issuance:
Date Issued: Feb. 27, 1984
Fact Sheet Number: 18

1. Description of Chemical

Generic Name: dimethyl N, N'-thiobis(methylimino) carbonyloxy bis ethanimidothioate

Common Name: thiodicarb

Trade Name: Larvin®

EPA Shaughnessy Code: 114501

Chemical Abstracts Service (CAS) Number: 900

Year of Initial Registration: 1984

Pesticide Type: insecticide

Chemical Family: carbamate

U.S. and Foreign Producers: Union Carbide Corporation

2. USE PATTERNS AND FORMULATIONS

Application Sites and Rates:

Thiodicarb is currently registered for use on sweet corn (fresh market only in the state of Florida). The application rates range from 0.5 lbs. active ingredient per acre to 0.75 lbs. active ingredient per acre per acre, not to exceed 7.5 lbs. active ingredient per acre per use season.

Types of Formulations:

Thiodicarb is commercially formulated into five (5) flowable products and one (1) wettable powder. There is also a 95% technical product federally registered.

Types and Methods of Application:

Application to sweet corn is made with both ground and air equipment.

3. Science Findings

Summary Science Statement

Thiodicarb is a cholinesterase inhibiting pesticide. Studies on the formulated products demonstrate a moderate toxicity to man (Toxicity Category II). The metabolism of thiodicarb is adequately understood. One of the metabolic by-products of thiodicarb in animals is acetamide, a potential carcinogen. Thiodicarb is not expected to leach and reach ground water or to bioaccumulate in the environment.

Chemical Characteristics:

Thiodicarb is a white crystalline powder with a slight sulfurous odor. It has a melting point of 173-174°C. Thiodicarb is stable in light and ambient conditions and unstable in alkaline conditions. Its main degradation product is methomyl.

Toxicology Characteristics:

Thiodicarb technical is moderately toxic (Toxicity Category II) via the oral and inhalation routes of exposure with LD_{50} values of 325 milligrams (mg)/kilogram (kg) and >0.32 mg/liter (L), respectively. The acute dermal LD_{50} for thiodicarb in rabbits is >2000 mg/kg (Toxicity Category III). Corneal opacity and conjunctival redness, chemosis and discharge were observed in the

eyes of rabbits administered 44 mg of thiodicarb; however, all lesions cleared by day 7.

The toxicological data submitted in support of the established tolerance for residues in or on sweet corn includes a 2-year rat feeding/oncogenicity study which was negative for oncogenic effects at the levels tested (1.0, 3.0 and 10.0 mg/kg/day) and had a cholinesterase (ChE) and chronic toxicity no-observed-effect level (NOEL) of 10.0 and 3.0 mg/kg/day, respectively; a mouse oncogenicity study which was negative at the levels tested (1.0, 3.0 and 10.0 mg/kg/day); a 6-month dog feeding study with a ChE and subchronic NOEL of 15.0 mg/kg/day; a rat teratology study which was negative at 30.0 mg/kg/day and had a fetotoxic NOEL of 3.0 mg/kg/day; a mouse teratology study which was negative at 200 mg/kg/day and also had a NOEL of 200 mg/kg/day for fetotoxicity; a 3-generation rat reproduction study with a NOEL of 10.0 mg/kg/day (HDT); and an acute delayed neurotoxicity study which was negative at 660 mg/kg. Studies on mutagenicity showed negative potential. Based on the 2-year rat feeding study with a chronic toxicity NOEL of 3.0 mg/kg/day and using a safety factor of 100, the acceptable daily intake (ADI) for humans is 0.03 mg/kg of body weight (bw)/day. The theoretical maximum residue contribution (TMRC) from the established tolerance on sweet corn utilizes 2.38 percent of the ADI.

The oncogenic potential of acetamide has been demonstrated

in four different studies, the first being a study conducted by F. I. Dessau and B. Jackson in 1955, where two groups of Rockland albino rats were treated with a 40% solution of acetamide at a rate of 4000 mg/kg (equivalent to 40,000 ppm for younger rats or 80,000 ppm for older rats) by intubation 5 days/week for a period of 117 days for Group I and 205 days for Group II. Histopathological examination showed cytologic irregularities consisting of a greater variability of cellular and nuclear size, giant nuclei, and the presence of numerous mitoses, some of unusual appearance. Benign hepatocellular adenomas were also found in 2 treated animals in Group II.

Doctors Dessau and Jackson conducted a second study in 1961, with 3 groups of Wister albino rats. The test duration was 12 months. Group I animals were administered via diet a 5% (50,000 ppm) solution of acetamide continuously. Group II animals were divided into three subgroups receiving 5%, 2.5% (25,000 ppm) and 1.25% (15,000 ppm) acetamide. Test material was administered in a diet of ground Wayne Laboratory Blox. Each week, two rats from treatment Group III were taken off the acetamide diet and placed on a control diet for the remainder of the testing period. Hepatomas were noted in four of forty eight animals in Group I, one of eighteen animals, six of twenty-two animals and four of twenty four animals tested in Group II, subgroups 1-3 respectively, and twenty-two of eighty one animals tested in Group III. In a study conducted by J. H. Weisburger, R. S. Yamamoto, R. M. Glass and H. H. Frankel

in 1969, 2 groups of male Wister rats were administered 2.5% (25,000 ppm) acetamide in a diet of Wayne Laboratory Blox. Group I animals were sacrificed after twelve months. Test animals in Group II were removed from the acetamide diet after twelve months and continued on a controlled diet for an additional three months. Animals in both test groups were administered 75 milligrams/liter of oxytetracycline (Terramycin) for one week every sixth week of the study. Hepatomas were noted in 2 of eight animals tested in Group I and 7 of sixteen animals tested in Group II. No effect was noted in the fifteen control animals.

The fourth study, a carcinogenesis bioassay of acetamide in rats and mice was conducted by R. W. Fleischman, et. al. in 1980. This study included 8 compound-dosage groups per sex for rats and 10 such groups for mice. Rats received 2.36% (23,600 ppm) of acetamide via diet. The mice were divided into two groups with Group I receiving 1.18% (11,800 ppm) of acetamide and Group II receiving 2.36% of acetamide. Test material was administered to animals in a diet of ground Wayne Lab Blox for a 12 month period and was then replaced with a controlled diet of Wayne Blox pellets for an additional 4 months. There were no apparent compound related effects noted in male and female mice. However, 41 liver carcinomas and 1 neoplastic nodule were noted in male rat test animals and 33 liver carcinomas and 3 neoplastic nodules were noted in female rat test animals.

The Agency has evaluated the four acetamide studies and have found the studies inappropriate for addressing the tumorigenicity potential of acetamide in accordance with today's standards for oncogenicity testing. Only a small number of male rats were used in 3 of the 4 studies in either the test groups or the controls or both. A single dietary level was administered to rats in 3 of the 4 studies which does not allow the determination of a dose related effect. In all studies, the exposure rates were extremely high which may have been responsible for the excessive weight loss and mortality noted in several of the studies. The administration of oxytetracycline (Terramycin) to test animals in the study conducted by Weisburger et. al. (1969) raises questions on the quality of the animals used and the possibility of adversely influencing the results of the experiment. A time related dose response which may or may not be real from a biological point of view was noted in the Dessau and Jackson study of 1961. Also the results of this study which indicated that there were no tumor effects in similar rats receiving a diet of acetamide in Purina Laboratory Chow versus effects in test animals receiving a diet of acetamide in ground Wayne Laboratory Blox casts doubts on the certainty of acetamide's oncogenic potential, as well as its potential hazard to humans. In the study conducted by R. W. Fleischman, et. al. in 1980, test animals (mice) used came from different lots and suppliers. Data describing weight gain, survival and intercurrent disease were not provided. Also, in this study

the number of tissues examined varied between study groups.

Based on the conduct of the available studies on acetamide and in consideration of the available oncogenicity testing in the rat and mouse for thiodicarb which demonstrated a negative oncogenic potential, the Agency has not determined that thiodicarb is oncogenic under normal agricultural practices. However, the Agency has conducted a risk assessment of the proposed tolerance request based on the four acetamide studies. The estimated maximum daily human exposure to acetamide from conversion of consumed thiodicarb residues is 1.4×10^{-4} mg/day for a 60 kg person and with an exposure risk of 3.07×10^{-3} the resulting life-time carcinogenic risk estimate is 7×10^{-9}. This life-time carcinogenic risk assessment is based on the following assumptions:

- Acetamide is presumed definitely to be carcinogenic.
- Carcinogenic effects noted in experimental animals at acetamide dietary levels of 10,000-80,000 ppm are applicable to humans exposed at a maximum level of 9.3 ppb.
- The mathematical relationship between dose and response that holds in the low dose region is based on the application of the one-hit model of carcinogenesis which yields the highest risk of any of the plausible models of dose response relations.
- The metabolic pathway of thiodicarb in humans is presumed to be the same as that found in test

animals and the highest value of risk obtainable from the animal data is applicable to humans.

- The conversion ratio of thiodicarb to acetamide in test animals is 306, based on metabolism studies, and this is the same in humans.
- Total production of sweet corn components in the United States will contain thiodicarb residues at the tolerance level.

Physiological and Biochemical Behavior Characteristics:

The metabolic pathway of thiodicarb in livestock has been demonstrated to be thiolysis to methomyl, followed by hydrolysis to the methomyl oxime and subsequent metabolization to acetonitrile. Acetonitrile is then metabolized to acetamide, a potential carcinogen, and further hydrolyzed to acetic acid which enters the intermediary metabolism cycle of the animal and is ultimately expired as carbon dioxide.

Plant metabolism studies show that thiodicarb is likewise metabolized to the methomyl oxime followed by acetonitrile and carbon dioxide, both of which are then volatilized.

Environmental Characteristics:

Thiodicarb is very stable at pH 6 and unstable in alkaline conditions. It is subject to decomposition by eight. The major by-product of photolysis is methomyl. Light textured soils causes more rapid degradation than heavy textured soils.

Thiodicarb exhibits low mobility in all soils. Degradation is also influenced by increasing temperatures, degree of aeration and microbial activity. The half-life on soil and plant surfaces is less than one week. Thiodicarb is non-persistent in the environment.

Ecological Characteristics:

Thiodicarb is moderately toxic to fish with a LC_{50} value of 2.55 ppm for the rainbow trout and 1.21 ppm for the bluegill sunfish. The avian acute LD_{50} for the bobwhite quail is 2023 ppm. The subacute dietary LC_{50} for the bobwhite quail and the mallard duck is 5620 ppm. The 48-hour acute LC_{50} for aquatic organisms is 0.0053 ppm.

Tolerance Assessment:

A tolerance of 2.0 parts per million (ppm) has been established to cover residues of thiodicarb and its metabolite methomyl in or on sweet corn grain (kernels plus cob with husk removed (K+WHR)) under the provisions of the Federal Food, Drug and Cosmetic Act (FFDCA). The 2.0 pm tolerance level is adequate to cover anticipated residues in or on sweet corn as a result of application under the currently registered use pattern.

4. Summary of Regulatory Position and Rationale:

Geographical Restrictions:

Thiodicarb is currently registered for use on sweet corn only. Products containing thiodicarb are also limited to application to sweet corn only in the State of Florida. Grazing and feeding

of treated corn fodder and forage is prohibited.

Summary of Risk Assessment

On the basis of the available studies on acetamide and the chronic oncogenicity studies for thiodicarb, the Agency has concluded that the human risks posed by the use of thiodicarb on sweet corn does not raise prudent concerns of unreasonable adverse effects.

5. Summary of Major Data Gaps

All data requirements have been addressed for thiodicarb. Therefore, all products containing thiodicarb have been unconditionally registered.

6. Contact Person at EPA

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